Docket-No.: 7003/45

| CKCL110 1000/10 | | |
|--|----------------------|------------------------|
| se type a plus sign (+) inside this box hor porter PTO/SB/08 | | |
| Substitute for form 1449/PTO | Comp | plete if Known |
| (بى JUL 3 1 2006 | Application Number | 10/550,856 |
| INFORMATION DISCLOSURE | Int'l Filing Date | 03/24/2004 |
| STATEMENT BY ARBITEANT | First Named Inventor | Stephen Ludwig, et al. |
| STATEMENT BRANDEDOANT | Group Art Unit | Unassigned 1654 |
| (use as many sheets as necessary) | Examiner Name | Unassigned Julie Ha |

of

4

| Examiner | Cite | U.S. Patent Document | | Name of Patentee or | Issue Date |
|---|-------|----------------------|----------|--------------------------------|---|
| Initials* | No. 1 | Number Class/S | Subclass | Applicant of Cited Document | MM-DD-YYYY |
| | | | | of Cited Document | |
| *************************************** | | | | | |
| | - | | | | *************************************** |

Attorney Docket Number

7003/45

| Exam iner Initial | Cite No. 1 | Office ³ | Foreign Patent De Number | ocument Class/ Subclass | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Т |
|-------------------------|---------------|---------------------|-----------------------------|----------------------------|--|--|---|
| - | | | | | | | |
| | | | | | | | |

| Examin er Initials* | Cite No. 1 | U.S. Patent Pul | Class/Subclass | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
|---------------------------|---|-----------------|----------------|---|---|
| milliona | *************************************** | | | | |
| | | | | | |

| | | OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | T-2 |
|-----------------------|---------------|---|-----|
| Examiner Initials* | Cite No. 1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | |
| /J.H./ | 1. | HEIKE FESQ, et al., "Programmed Cell Death (Apoptosis) in Human Monocytes Infected by Influenza A Virus, <i>Immunobiol.</i> , 1994, vol. 190, pp. 175-182. | |
| /J.H./ | 2. | ISAMU MORI, et al., "In Vivo Induction of Apoptosis by Influenza Virus", Journal of General Virology, 1995, vol. 76, pp. 2869-2873. | |
| /J.H./ | 3. | TAKENORI TAKIZAWA, et al., "Induction of Programmed Cell Death (Apoptosis) by Influenza Virus Infection In Tissue Culture Cells", <i>Journal of General Virology</i> , 1993, vol. 74, pp. 2347-2355. | |

| Examiner Signature | /Julie Ha/ | Date Considered | 05/20/2008 | |
|-----------------------|------------|--------------------|------------|--|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered, include copy of this form with next communication to applicant.

¹²Unique citation designation number. ²Applicant is to place a check mark here if English language Translation is attached.
Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer. Fatent and trademark Office, Washington, DC 20231.
DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Docket No.: 7003/45

Please type a plus sign (+) inside this box. FORM PTO/SB/08

| Substitute for | orm 1449A/PTO | | | Compl | ete if Known |
|----------------|----------------|------|-----------|------------------------|------------------------|
| | | | | Application Number | 10/550,856 |
| INFOE | MATION D | 120 | OSURE | Int'l Filing Date | 03/24/2004 |
| | EMENT BY | | | First Named Inventor | Stephen Ludwig, et al. |
| SIAII | EMENIBI | API | LICANI | Group Art Unit | -Unassigned 1654 |
| (use | as many sheets | as n | ecessary) | Examiner Name | Unassigned Julie Ha |
| Sheet | 9 | of | 4 | Attorney Docket Number | 7003/45 |

| | | OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | T ² |
|---------------------|--|---|----------------|
| xaminer nitials* | Cite No. 1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | |
| /J.H./ | 4. | HANA VAN CAMPEN, et al., "Virulent Avian Influenza A Viruses: Their Effect on Avian Lymphocytes and Macrophages <i>in vivo</i> an <i>in vitro</i> ", <i>J. Gen. Virol.</i> , 1989, vol. 70, pp. 2887- 2895. | |
| | 5. | HANA VAN CAMPEN, et al., "Destruction of Lymphocytes by a Virulent Avian Influenza A Viruses", J. Gen. Virol., 1989, vol. 70, pp. 467-472. | |
| | 6. | LARISA V. GUBAREVA, et al., "Evidence for Zanamivir Resistance in an Immunocompromised Child Infected with Influenza B Virus", <i>The Journal of Infectious Diseases</i> ", 1998. vol. 178, pp. 1257-1262. | |
| | 7. | C. SCHOLTISSEK, et al., "Failure to Obtain Drug-Resistant Variants of Influenza Virus After Treatment with Inhibiting Doses of 3-Deazaadenosine and H7", Archives of Virology, 1991, vol. 119, pp.111-118. | |
| | 8. | PHILLIP D. ZAMORE, et al., "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals", Cell, March 31, 2000, vol. 101, pp. 25-33. | |
| | YUICHI WATANABE, et al., "Role of Phosphatidylserine Exposure and Sugar Ch Desialylation at the Surface of Influenza Virus-Infected Cells in Efficient Phagooy Macrophages", The Journal of Biological Chemistry, Issue of May 17, 2002, vol. 20, pp. 18222-18228. | | |
| | 10. | THOMAS TUSCHL, et al., Targeted mRNA Degradation by Double Stranded RNA in Vitro, downloaded from www.genesdev.org on April 13, 2006, pp. 3190-3197. | |
| /J.H./ | 11. | TERRANCE M. TUMPEY, et al., "Depletion of Lymphocytes and Diminished Cytokine Production in Mice Infected with a Highly Virulent Influenza A (HSN1) Virus Isolated from Humans", Journal of Virology, July 2000, vol. 74, no. 13, pp. 6105-6116. | |

| Examiner /Julie Ha/ Date Considered 05/20/2008 | | | |
|--|------------|---|------------|
| | /Julie Ha/ | • | 05/20/2008 |

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹²Unique citation designation number. ²Applicant is to place a check mark here if English language Translation is attached.
Burden Hou Statement. This form is estimated to take 2.0 hours to complete. Time will vary depending upon the reads of the individual case. Any comments on the amount of time you are required to complete this from should be sent to the Chief Information Officer, Patent and trademark Office, Washington, DC 20231.
DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO. Assistant Commissioner for Patents, Washington, DC 20231.

Docket No.: 7003/45

Please type a plus sign (+) inside this box. FORM PTO/SB/08

| Substitute for | form 1449A/PTO | | | Complete if Known | | | |
|------------------------|----------------|----------------------|------------------------|------------------------|---------------------|--|--|
| | | | | Application Number | 10/550,856 | | |
| INFO | RMATION D | ISC | OSURE | Int'l Filing Date | 03/24/2004 | | |
| STATEMENT BY APPLICANT | | First Named Inventor | Stephen Ludwig, et al. | | | | |
| SIAI | EMENI DI | AF | LICANI | Group Art Unit | Unassigned 1654 | | |
| (use | as many sheets | as ne | ecessary) | Examiner Name | Umassigned Julie Ha | | |
| Sheet | 3 | of | 4 | Attorney Docket Number | 7003/45 | | |

| | | OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS | |
|-----------------------|---------------|--|----------------|
| Examiner Initials* | Cite No. 1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc., date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ² |
| ^ /J.H./ | 12. | NANCY A. THORNBERRY, et al., "Caspases: Enemies Within", Science, August 28, 1998, vol. 281, pp. 1312-1316. | |
| | 13. | MUNEESH TEWARI, et al., "Yama/CPP32β, a Mammalian Homolog of CED-3, is a CrmA-Inhibitable Protease that Cleaves the Death Substrate Poly(ADP-Ribose) Polymerase", Cell, June 2, 1995, vol. 81, pp. 801-809. | |
| | 14. | STEPHAN PLESCHKA, et al., "A Plasmid-Based Reverse Genetics System for Influenza A Virus", <i>Journal of Virology</i> , June 1996, pp. 4188-4192. | |
| | 15. | STEPHAN PLESCHKA, et al., Influenza Virus Propagation is Impaired by Inhibition of the Raf/MEK/ERK Signalling Cascade", <i>Nature Cell Biology</i> , March 2001, vol. 3, 7 pages. | |
| | 16. | CHRISTOPHER W. OLSEN, et al., "bcl-2 Allers Influenza Virus Yield, Spread, and | |
| | 17. | ROBERT E. O'NEILL, et al., "The Influenza Virus NEP (NS2 Protein) Mediates the Nuclear Export of Viral Ribonucleoproteins", <i>The EMBO Journal</i> , 1998, vol.17, no. 1, pp. 288-296. | |
| V | 18. | STEPHEN LUDWIG, et al., "Influenza Virus-Induced AP-1-Dependent Gene Expression Requires Activation of the JNK Signaling Pathway", <i>The Journal of Biological Chemistry</i> , vol. 276, no.14, issue of April 6, 2001, pp. 10990-10998. | |
| /J.H./ | 19. | STEPHEN LUDWIG, et al., "Influenza A Virus NS1 Protein Inhibits Activation of Jun N- Terminal Kinase and AP-1 Transcription Factors", Journal of Virology, vol. 76, no. 21, Nov. 2002, pp. 11166-11171. | |

| Examiner /Julie Ha/ Date Considered 05/20/2008 | | | |
|--|-----------------------|------------|------------|
| | Examiner Signature | /Julie Ha/ | 05/20/2008 |

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹³Unique citation designation number. ²Applicant is to place a check mark here if English language Translation is attached. Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Intomation Officer, Palent and trademark Office, Washington, DC 20231. DO NOT SEND PEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231. Docket No.: 7003/45

Please type a plus sign (+) inside this box. FORM PTO/SB/08

| Substitute for form 1449A/PTO | | | | Complete if Known | | | |
|-----------------------------------|-----------|------|-----------|------------------------|------------------------|-------|----|
| | | | | Application Number | 10/550,856 | | |
| INFO | RMATION D | oisc | LOSURE | Int'l Filing Date | 03/24/2004 | | |
| STATEMENT BY APPLICANT | | | | First Named Inventor | Stephen Ludwig, et al. | | |
| | | | | Group Art Unit | -Unassigned | 1654 | |
| (use as many sheets as necessary) | | | ecessary) | Examiner Name | Umassigned | Julie | Ha |
| Sheet | 4 | of | 4 | Attorney Docket Number | 7003/45 | | |

| | | OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS | Τ² | | | |
|---|-----|--|----|--|--|--|
| Examiner Initials* Cite No. 1 20. /J.H./ | | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, ect), date, pagedy, wolume-issue number(s), publisher, city and/or country where published. REINER U. JÄNICKE, et al., "Caspase-3 is Required for DNA Fragmentation and Morphological Changes Associated with Apoptosis", The Journal of Biological Chemistry, vol. 273, no.16, issue of April 17, 1998, pp. 9357-9360. | | | | |
| | | | | | | |
| | 22. | LAVINA FALEIRO, et al., "Caspases Disrupt the Nuclear-Cytoplasmic Barrier", The Journal of Cell Biology, vol. 151, no. 5, November 27, 2000, pp. 951-959. | | | | |
| | 23. | QUINN L. DEVERAUX, et al., "X-Linked IAP is a Direct Inhibitor of Cell-Death Proteases", Nature, vol. 388, July 17, 1997, pp. 300-304. | | | | |
| | 24. | GERALD M. COHEN, "Caspases: The Executioners of Apoptosis", <i>Biochem J.</i> , 1997, vol. 326, pp. 1-16. | | | | |
| T | 25. | WEISAN CHEN, et al., "A Novel Influenza A Virus Mitochondrial Protein That Induces Cell Death", Nature Medicine, December 2001, vol. 7, no.12, pp. 1306-1312. | | | | |
| | 26. | THIJN R. BRUMMELKAMP, et al., "A System for Stable Expression of Short Interfering RNA's in Mammalian Cells", Science, April 19, 2002, vol. 296, pp. 550-553. | | | | |
| /J.H./ | 27. | SIDDHARTH BALACHANDRAN, et al., "Alpha/Beta Interferons Potentiate Virus-Induced Apoptosis Through Activation of the FADD/Caspase-8 Death Signaling Pathway", Journal of Virology, February 2000, pp. 1513-1523. | | | | |

| Examiner Signature | /Julie Ha/ | Date Considered | 05/20/2008 |
|-----------------------|------------|--------------------|------------|
| | | | |

^{*}EXAMINER: initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

^{**}Indique citation designation number: *Applicant is to place a check mark here if English language Translation is attached. Butden Hord Statement: This form is estimated to take 2.0 hours to complete. Time will very depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and trademark Office, Washington, DC 20231.
DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington CD 20231.